REMARKS

I. Status of the Claims

Claims 245-248, 251, 253, 261-265, 306 and 307 were pending and examined in the August 17, 2010 Office Action. Claims 247, 248, 251, 253, 261-265, 306 and 307 are canceled herewith. Claims 245 and 246 are presented for reconsideration.

I. Double Patenting Rejections

Claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 275, 289, 290 and 296-301 of copending Application No. 08/978,634. Additionally, claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of ODP as being unpatentable over claims 1 and 3-5 of copending Application No. 11/929,897. Since these rejections are dependent on the scope of the final claims in both the instant application and applications 08/978,634 and 11/929,897, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

II. Rejection under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 245-248, 251, 253, 261-265, 306 and 307 are rejected under 35 U.S.C. 112, first paragraph, written description requirement. Applicants request reconsideration and withdrawal of this rejection in light of the following discussion.

In addition to the specification disclosure discussed in Applicants' Reply dated February 17, 2011, the current claims precisely describe the compositions illustrated in FIGS. 4 and 6, including the relationship of the various components, except an antibody replaces the fusogenic peptides in FIG. 4 or the Segment 4 of FIG. 6b. Those embodiments are also discussed at para. **[0117]**, **[0124]**-**[0125]** and **[0159]**-**[0161]** of the specification as published as US 2001/0006814. As discussed therein, the antibody component is useful for cell targeting. Construction of the claimed embodiments is

provided, for example in FIG. 5 and para. **[0383]** – **[0395]**. In light of the specification disclosure discussed above and in the February 17, 2011 Reply, it is clear that the specification describes specific components of the construct that is sufficient to adequately describe the distinguishing features and attributes concisely shared by all members of the claimed composition.

The current Office Action and the previous Office Action dated August 17, 2010 assert that "...the disclosure fails to provide a representative number of species for such a broad genus that would provide the claimed function of cell delivery to any cell in an organism in vivo or in vitro." Applicants disagree, since the claimed genus is not broad since claim 245 describes very specifically the structure illustrated in FIG. 4, where an antibody replaces the fusogenic peptides in that illustration.

The Office Action also asserts that "...the skilled artisan would not know how big the first nucleic acid strand would need to be such that a second nucleic acid strand is fully complementary and is capable of forming a double stranded structure that is a template for synthesis of any nucleic acid product." Applicants again disagree with this assertion, since the skilled artisan would understand that the size and details of useful examples of the claimed circular structure could certainly be ascertained by evaluating the extraordinarily vast literature present at the time of filing on the size and structure of natural and artificial plasmids, which are circular nucleic acids having an array of sizes that, at the time of filing, has collectively provided templates for synthesis of an immense number of nucleic acid products. Indeed, the claimed composition could be considered to be a modified plasmid. In that regard, the skilled artisan would understand that teachings provided in the massive plasmid literature at the time of filing could be utilized to provide answers to any questions that might arise about details of the claimed compositions that are not provided in the specification, for example as posed by the Office (e.g., "How many nucleotide residues are required for inter-strand hybridization to keep the proposed constructs intact in a cell, or prior to being taken up by a target cell in an organism?"). As such, the skilled artisan would understand that

the claimed composition could be utilized without undue experimentation to produce any nucleic acid product that a plasmid could produce.

In view of the claim amendments and the above discussion, withdrawal of the written description rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

III. Rejection under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 245-251, 253, 261-265, 306 and 307 are rejected under 35 U.S.C. 112, first paragraph, enablement requirement. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the following discussion.

The Office Action dated August 17, 2010 admits that the specification is enabling for the "...self-annealing, multi-component systems in schematics as illustrated in Figures 4, 6, 15-18...." As such, the claimed compositions should be deemed enabled since the claimed compositions are the compositions illustrated in FIG. 4 and 6, except an antibody replaces the fusogenic peptides in FIG. 4.

That Office Action also cites several references purporting to teach the lack of enablement of antisense and ribozyme therapeutics. In response, Applicants first note that the instant claims are directed to a composition and not to any therapeutic application with that composition. As such, the composition as claimed need not be enabled for effectively treating every, or even any particular disease or condition using every, or even any particular nucleic acid product. The skilled artisan would understand that the composition is undoubtedly fully enabled for use in a cell *in vitro* since its modified plasmid configuration (as discussed under **II.** above) indicates that it would behave like a plasmid, with the added feature that the antibody can assist in cell targeting. Further, the PTO is being inconsistent in asserting that the claimed compositions are not effective in cells or whole organisms, due, e.g., to the ineffectiveness of an antisense or ribozyme encoded therein, since the PTO has issued numerous patents, filed before the priority date of the instant application, claiming such a use. See, e.g., 5,635,385; 5,908,779; 6,451,603; 7,326,783; and 5,990,088.

In citing six references (Crooke, Peracchi et al., Agrawal et al., Chirila et al., Opalinska et al., and Jang et al.) in the August 17, 2010 Office Action, the PTO attempts to assert that the claims are not enabled based on potential applications (e.g., antisense and ribozyme therapeutics) to which the claimed compositions could be used. However, Applicants note that

> The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling).

MPEP 2164.08(b). Thus, the claim is not rendered nonenabled even if it encompasses the use of a particular nucleic acid product expressed from the claimed composition that might not be an effective treatment for a particular disease or condition in a particular organism, since the skilled artisan could determine without undue experimentation whether any particular application would be effective, by, e.g., referencing the plasmid literature, since the claimed composition is a modified plasmid.

The above MPEP quote is also notes that "prophetic examples do not make the disclosure nonenabling." In this regard, Applicants need not provide a non-prophetic example of the use of the instant compositions, since the skilled artisan could make and use the claimed composition without undue experimentation and could determine whether any particular parameter, e.g., the length of each particular nucleic acid strand, the amount of complementarity to the first nucleic acid strand that need be present in the second nucleic acid strand, etc. is effective in the composition. Again, such knowledge could easily be gleaned from the extensive literature on plasmids.

Applicants also assert that the references cited in the August 17, 2010 Office Action are irrelevant to the enablement of the claimed composition. Two of the references (Peracchi and Agrawal et al.) question the ability of oligonucleotides to enter cells. Those references are irrelevant to enablement of the instant compositions since the gene product from the instant composition is expressed after the composition

already enters the cell, so a ribozyme or antisense oligonucleotide expressed from the claimed composition in a cell would not have the problem of having to enter the cell. Further, as discussed under **II.** above, the antibody portion of the composition assists in the targeting and entry of the composition into cells. Also, the vast literature relating to entry of plasmids into cells would provide direction for any cell targeting issues with any particular embodiment of the claimed composition.

A third reference cited in the August 17, 2010 Office Action, Crooke, is cited to indicate that dose-response curves should be carefully evaluated when an antisense therapeutic is being moved from *in vitro* to *in vivo* experiments. This is also completely irrelevant to the enablement of the instant compositions since it does not address any issue regarding the enablement of the claimed compositions. Similarly, Opalinska et al. is cited to indicate that nucleic acid therapy is unpredictable, which also does not address any issue regarding the enablement of the claimed compositions. The final cited reference, Jang et al. relates to the unpredictability of nucleic acid delivery devices, which is also clearly irrelevant to the claimed compositions, which do not include any delivery device. Thus, none of the references cited in the August 17, 2010 Office Action are at all relevant to the claimed compositions.

Based on the above discussion, the claimed compositions are enabled since they are modified plasmids, such that the plasmid literature could be utilized to provide the skilled artisan the ability to effectively make and use the claimed compositions. Additionally, the utility and effectiveness of the antibody moiety would be understood since the prior art teaches that antibodies attached to nucleic acids are useful for targeting the nucleic acid to a cell. See, e.g., US Patents 5,521,291 and 5,391,723, which were cited in the Office Action dated November 23, 2009 for that teaching.

In view of the above discussion, Applicants assert that the claims are enabled for their full scope. Withdrawal of the enablement rejection under 35 U.S.C. 112, first paragraph, is therefore respectfully requested.

IV. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of rejections of record and passage of the claims to allowance.

The United States Patent and Trademark Office is hereby authorized to charge the extension of time and Request for Continued Examination fees, as well as any other fees required to maintain pendency of this application, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

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